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1339730

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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

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☑ *Additional inventors are being named on the* 1 *separately numbered sheets attached hereto*

TITLE OF THE INVENTION (500 characters max)

EXACTLY DIVIDABLE, LAYERED, SCORED TABLET

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ENCLOSED APPLICATION PARTS *(check all that apply)*

☑ Specification *Number of Pages* 11
☑ Drawing(s) *Number of Sheets* 1
☐ Application Data Sheet. See 37 CFR 1.76
☐ CD(s), Number
☐ Other (specify)

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Respectfully submitted,

SIGNATURE _____

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Date 05/21/2004

REGISTRATION NO. *(if appropriate)* 52,737

Docket Number: 1322-013

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PROVISIONAL APPLICATION COVER SHEET
Additional Page

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Docket Number	1322-013

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Number 2 of 2

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UNITED STATES PATENT APPLICATION
(PROVISIONAL)

of

Lawrence Solomon

and

Allan Kaplan

EXACTLY DIVIDABLE, LAYERED, SCORED TABLET

1322-013

EXACTLY DIVIDABLE, LAYERED, SCORED TABLET

FIELD OF THE INVENTION

The invention is concerned with the making of a tablet dosage form for the administration of pharmaceuticals or other materials. The novel scored tablets of the invention may be readily and accurately separated into separate parts which contain predetermined quantities of ingredients.

BACKGROUND OF THE INVENTION

It is well known to provide tablets for handling pre-measured quantities of materials which allow consumers to use various materials without the need to use expensive and cumbersome measuring devices. Tablets have been used to prepare measured amounts of herbicides, pool-treating chemicals, pigments, pharmaceuticals and other solid products which are used in measured amounts. It is common with these tablets to form the tablet with an indentation, commonly referred to as a "score," that is sized and positioned to enable an end user to break the tablet into one or more components. It is recognized that heretofore a method of producing complete, accurate, and predictable division of active ingredient(s) in a tablet has not been disclosed.

Many drugs require dosage adjustments. Tablets such as warfarin are scored and are highly potent and patients are frequently advised by physicians to divide warfarin tablets to effect dosage adjustments. If a patient divides a tablet of this drug, the result is likely to not be an exact division of the tablet. The resultant imprecise dosing may cause adverse medical consequences.

SUMMARY OF THE INVENTION

The present invention is concerned with a dosage form containing at least two layers, in which at least one layer is conveniently and precisely dividable into sections, by means of one or more scores that extend substantially to an adjacent layer. The dosage form preferentially comprises a layered structure composed of two adjacent layers, one containing the active ingredient or mixture of active ingredients (layer 2) and the other containing either an inert substance or one or more active substances (layer 4), wherein layer 2 is fully breakable in an exact, predetermined manner (such as into two equal halves), whereas layer 4 does not break fully evenly. The reason that layer 2 can be broken into exactly equal halves is that it has a score that extends A) substantially completely into layer 4 or B) substantially to layer 4. Thus, if the tablet is broken, the break will take place A) only or B) substantially only in layer 4.

The invention also includes the method of administering a pharmaceutical to a patient which comprises administering a dosage form comprising a layered structure having two or more layers, wherein the first layer comprises active ingredient(s) and the second layer comprises inert ingredients, or one or more active ingredients. Said first layer being completely scored to allow it to separate precisely into two or more parts of predetermined amount of active ingredient(s)when the tablet is broken through the score(s).

The invention further contemplates that the method of breakage may be manual, but manual breakability is not required if mechanical breakage may be conveniently

accomplished by ordinary means such as by utilizing a commercially-available tablet cutter, a kitchen knife, or a penknife ("manual or mechanical").

It is contemplated that should it be desired that layer 4 contain active drug, and there be physical incompatibility between any component of layer 2 with layer 4, a thin separating layer, as is well known in the art, may be placed between layers 2 and 4 that is mutually compatible with each layer. In that case, the score of layer 2 will extend substantially at least to the separating layer (not shown), and possibly into layer 4. For convenience, the term "inert layer" when applied to a two-layer tablet hereafter, is intended to encompass the circumstance in which layer 4 as used above contains active drug(s) and is not inert.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

Fig. 1 is a side view of a cross-section of a two-layer scored tablet according to the invention, which shows an embodiment in which the score terminates at the interface of the active and inert layers.

Fig. 2 is a side view of a cross-section of a two-layer scored tablet according to the invention, which shows an embodiment in which the score extends through the active layer and into the inert layer.

Fig. 3 is a side view of a cross-section of a two-layer scored tablet according to the invention, which shows an embodiment in which the score extends through the interface of the active layer into the inert layer and a reinforcing ridge has been formed as part the inert layer.

Fig. 4 is a top view of a two-layer scored tablet according to the invention which has been scored into four sections.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is particularly useful when precise dosing is important and patients undergo dosage adjustments from time to time.

Examples of these drugs includes, nonexclusively, warfarin, digoxin, digitoxin, and l-thyroxine.

As shown in Fig. 1, the active layer 2 is placed against layer 4 and score 6 is created to extend completely through the active layer to but not into the inert layer. This arrangement allows the active layer to be divided into two exact sections because the break occurs at the interface of the inert and the active layers in such a manner that the portions of the tablet containing the active drug are completely and exactly separable. While this embodiment is a tablet in which the active layer is divided into two parts, it is also possible to provide three or more scores that extend up to or into the inert layer.

Fig. 2 varies from Fig. 1 in that the score extends into layer 4.

Fig. 3 varies from Fig. 2 in that a reinforcing ridge 12 is created as part of layer 4 in register with ridge 6 to help protect the tablet from breakage.

Fig. 4 is a top view of an embodiment of the invention in which the tablet is scored to provide sections 14, 16, 18 and 20. Shading 22 is used to show the sloping

walls of the scores while line 24 shows the bottom of the score mark.

The drawings illustrate the scores as being V-shaped but the shape of the scoring profile is not critical to the scope of the invention, and the invention includes scores having any type of profile that allow the precise division of the active layer without regard to the accuracy of the division of the remainder of the tablet.

It is contemplated that the different layers may either have the same or different colors.

The tablets may be made using conventional ingredients such as those disclosed in standard textbooks such as Remington's Pharmaceutical Sciences, 17th Ed.(1985) pp. 1603-1632, which are incorporated by reference.

The technique of making the tablets may comprise first feeding a granulation of the inert component into a tablet die and tamping the granulation into place. Then, a granulation of the active drug is placed on top of the tamped inert granulation and an embossed die having the reverse configuration of a score mark(s) is applied to the top of the granulation of the active ingredient to form the tablet with a groove or grooves (or score(s)) being pressed into the active layer by the embossed die as described above.

As examples, layer 2 may contain one or more of the following, and layer 4 may be substantially inert or may contain one or more of the following as well.

The following list discloses a variety of active pharmaceutical ingredients which could be given singly or in combination either in layer 2 or layer 4, with layer 4 in the invention's more preferred embodiment containing no

active drug. These examples are a small subset of the possible examples, which comprise substantially every tabletable drug or drug combination that has existed, is in existence, or that may come to exist.

HYPOGLYCEMIC AGENTS:
Thiazolidinediones: Pioglitazone, rosiglitazone
Sulfonylureas: Glyburide, glipizide, glimepiride, chlorpropamide
Biguanides: Metformin
Meglitinides: Nateglinide, repaglinide
Glucosidase inhibitors: Acarbose, miglitol

ANTIHYPERTENSIVE AGENTS:
Beta-blockers:
Acebutolol, atenolol, bisoprolol, celiprolol, metoprolol, mebivolol, carvedilol (a mixed alpha-beta blocker), nadolol, oxprenolol, penbutolol, pindolol, propranolol, timolol, betaxolol, carteolol,

Calcium antagonists (calcium-channel blockers):
Nifedipine, amlodipine, verapamil, diltiazem, nisoldipine, felodipine, isradipine, lacidipine, lercanidipine, nicardipine, manidipine

Thiazide-type diuretics (with or without potassium-retaining diuretics such as triamterene, amiloride, spironolactone, etc.):
Hydrochlorothiazide, chlorothiazide, cyclopenthiazide, polythiazide, bendrofluazide, hydroflumethiazide, chlorthalidone, indapamide, methylclothiazide, metolazone

Angiotensin converting enzyme inhibitors:

Captopril, enalapril, lisinopril, ramipril, trandolapril, quinapril, perindopril, moexipril, benazepril, fosinopril

Angiotensin receptor blockers:
Losartan, valsartan, candesartan, telmisartan, eprosartan, irbesartan

High-ceiling (loop) diuretics (with or without potassium-retaining diuretics such as triamterene, amiloride, spironolactone, etc.):
Furosemide, torsemide, ethacrynic acid, bumetamide

Aldosterone antagonist diuretics:
Spironolactone, eplerenone

Alpha-blockers:
Doxazosin, terazosin, prazosin, indoramin, labetolol (a mixed alpha-beta blocker)

Central alpha-agonists:
Clonidine, methyldopa

Imidazoline:
Moxonidine

Direct vasodilators:
Hydralazine, minoxidil
Adrenergic neuronal blocker:
Guanethidine

LIPID-MODIFYING AGENTS:

A) Statins:
Lovastatin, simvastatin, pravastatin, rosuvastatin, atorvastatin, fluvastatin

B) Fibrates:
Clofibrate, bezafibrate, fenofibrate, gemfibrozil, ciprofibrate

C) Others:
Ezetimide, niacin, acipimox

While certain preferred and alternative embodiments of the invention have been set forth for purposes of disclosing the invention, modifications to the disclosed embodiments may occur to those who are skilled in the art. Accordingly, this specification is intended to cover all embodiments of the invention and modifications thereof which do not depart from the spirit and scope of the invention.

Claims:

1. A dosage form comprising a structure consisting of at least two stratified layers of different composition, wherein a layer comprises one or more active ingredients and is exactly and predictably dividable by a scoring pattern placed into or substantially to an adjacent layer which is substantially an inert layer, or contains one or more active ingredients.

2. A dosage form as defined in claim 1 wherein the score extends completely through the active layer and ends at the interface between the active layer and the inert layer.

3. A dosage form as defined in claim 1 wherein the score extends completely through the active layer and past the interface between the active layer and the inert layer so that the score ends in the inert layer.

4. A dosage form as defined in claim 1 wherein the unscored or incompletely scored layer contains active drug or drugs.

5. A dosage form as in claim 4 wherein an inert separating layer exists and the unscored or incompletely scored layer contains active drug(s).

6. A method of administering a pharmaceutical to a patient which comprises administering a dosage form as in claim 1, wherein a first layer comprises one or more active ingredients and is exactly and predictably dividable by a scoring pattern placed into or substantially to an

adjacent layer which is substantially an inert layer, or contains one or more active ingredients.

7. A method as defined in claim 6 wherein the score in the dosage form extends completely through the active layer and ends at the interface between the active layer and the inert layer.

8. A method as defined in claim 6 wherein the score in the dosage form extends completely through the active layer and past the interface between the active layer and the inert layer so that the score ends in the inert layer.

9.A method as defined in claim 6 wherein the unscored or incompletely scored layer of the dosage form contains active drug or drugs.

10. A method as defined in claim 6 wherein the dosage form has an inert separating layer and the unscored or incompletely scored layer contains active drug.

ABSTRACT

A dosage form comprising a structure consisting of at least two stratified layers of different composition, wherein a layer comprises one or more active ingredients and is exactly and predictably dividable by a scoring pattern placed into or substantially to an adjacent layer which is substantially an inert layer, or contains one or more active ingredients.

1322-013

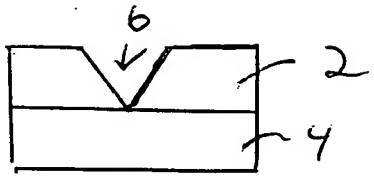

FIG. 1

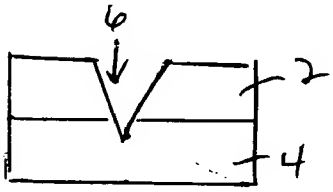

FIG. 2

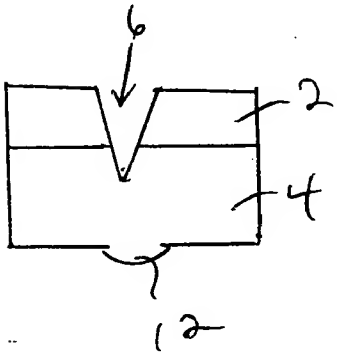

FIG. 3

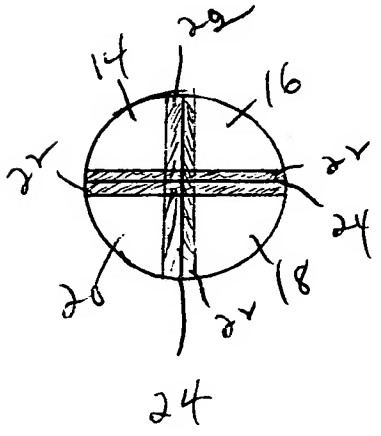

FIG. 4